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10/020,445	10/24/2001	Avi J. Ashkenazi	GNE.2630P1C74	9983

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EXAMINER	
SEHARASEYON, JEGATHEESAN	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/020,445	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *58-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *05/03 & 06/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 58-77 are pending and under consideration.

Specification

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

3. The disclosure is objected to because of the following informalities:

Applicants are advised that the ATCC has moved from Rockville, MD to Manassas, VA, effective March 23, 1998. The correct address is now:

American Type Culture Collection

10801 University Boulevard

Manassas, VA 20110-2209

Appropriate correction is required.

Information Disclosure Statement

4. The information disclosure statements, filed on 5/25/2002 and 6/13/2003, have been considered. The BLAST results demonstrate that applicants are aware of nucleic acids with identity/homology to the one claimed herein. However, as the BLAST results do not give sufficient identifying information, the Examiner cannot determine if said sequences constitute prior art.

Priority Determination

5. The utility for the claimed nucleic acids is based upon Example 114, at pages 331-346, in which it is shown that PR0615 nucleic acid is amplified atleast 2-fold in numerous human tumor cell lines. The earliest disclosure of this result that can be

confirmed by the Examiner is in US Application 60/131445, filed 4/28/99 (see pages 91-95, Table 3).

Should the applicant disagree with the examiner's factual determination above, it is incumbent upon the applicant to provide the serial number and specific page number(s) of any parent application filed prior to the date recited above which specifically supports the particular claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession of and fully enabled for prior to that date.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 58-77 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6a. Claims that recite "the extracellular domain" of the protein are indefinite as no extracellular domain has been described. Therefore, the metes and bounds of the claims cannot be determined. For example, see Claim 58-63, parts (c) and (d). Further, if the protein had an extracellular domain, the recitation of "the extracellular domain"..."lacking its associated signal sequence" (claim 58, part (d), for example) is indefinite as a signal sequence is not generally considered to be part of an extracellular domain, as signal sequences are cleaved from said domains in the process of secretion from the cell.

6b. Claims that recite that the claimed nucleic acid "hybridizes to" another sequence, such as claim 71, are indefinite as there is no limiting definition of such in the specification, and the metes and bounds of that which will hybridize are dependent upon the conditions under which the hybridization is performed. As the metes and bounds of what will hybridize to a given sequence are entirely dependent upon the conditions of hybridization and washing, the metes and bounds of the claims cannot be determined. With respect to claim 72, although the further limitation that the hybridization conditions are "stringent" is introduced, the term "stringent conditions" is also a relative term, and the metes and bounds of the claim cannot be determined.

The remaining claims are rejected for depending from an indefinite claim.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7a. Claims 58-62 and 71-77 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the nucleic acid of SEQ ID N0: 161 or fragments of such that are usable as hybridization probes, does not reasonably provide enablement for nucleic acids 80, 85, 90, 95 or 99% identical to such, nor which encode a protein 80, 85, 90, 95 or 99% identical to the protein of SEQ ID NO: 162, nor nucleic acids which hybridize to any of the above. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to:
1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re *Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims are directed to isolated nucleic acids having at least 80% identity to a SEQ ID NO: 161 or that encode the protein of SEQ ID NO: 162 with or without its signal peptide, or which encode the extracellular domain of SEQ ID NO: 162 with or without its signal peptide, or nucleic acids at least 80% identical to such encoding nucleic acids. Dependent claims are directed to vectors and host cells comprising the isolated nucleic acids. The specification contains numerous asserted utilities including use as hybridization probes, in chromosome and gene mapping, in the generation of anti-sense RNA and DNA, to identify molecules that bind to PRO615 (including agonists and antagonists), to make "knock-out" mice or other animals, in gene therapy, as molecular weight markers, therapeutic agents, and for the production of antibodies. None of these asserted utilities is specific for the disclosed PRO615 nucleic acids or protein, as each of the aforementioned utilities could be asserted for any naturally occurring protein, and further, as none of the asserted utilities requires any feature or activity that is specific to the disclosed PRO615.

Since the claimed nucleic acids are described at least in part in terms of the protein that might be encoded, the scope of the protein itself must be considered: The specification teaches that PRO615 has (unspecified) homology to "the Synaptogyrin protein, thereby indicating that PRO615 may be a novel Synaptogyrin." (See page 14 of the specification.) However, the "Synaptogyrin family" of proteins does not possess a common utility, but rather the proteins that can be broadly classified as Synaptogyrin have different activities, that confer different uses on them. Accordingly, the mere identification of a protein as belonging to a family, while indicative of evolutionary relatedness, is not indicative of function, nor by extension, of utility. At page 202, the specification states that "PRO615 polypeptides and portions thereof, which have homology to Synaptogyrin proteins, may also be useful for *in vivo* therapeutic purposes, as well as for various other applications. Given the medical importance of synaptic transmission, these molecules appear to play important roles in a number of disease processes "such proteins may serve as potential therapeutics for a variety of different human disorders," and "may also play important roles in biotechnological and medical research as well as various industrial applications." However, this statement is conjectural, and is merely an invitation to experiment to determine a utility for the protein. The structure of the putative PRO615 peptide is discussed at pages 252 as having a type II transmembrane domain, corresponding to about amino acids 24-43, other transmembrane domains, corresponding to about amino acids 74-90, 108-126 and 145-161, respectively, and potential N-glycosylation site, corresponding to about amino acids 97-100. However, there is no functional characteristic associated with

these motifs, hence the mere observation that they exist is not probative of function or utility. Further, there is no disclosure that the protein is expected to be a transmembrane protein, nor of any extracellular domain. As the protein itself has no utility, enablement is not commensurate in scope with claims to nucleic acids that are described structurally by their ability to encode such proteins.

The specification also is not enabling of the breadth of claims to nucleic acid molecules that hybridize to the disclosed sequences. It is noted that claims that recite hybridization language are indefinite, and do not recite that the nucleic acid encode a protein, much less one having a specifically disclosed activity. First of all, it is pointed out that the term "hybridize" or "hybridization" generically refers to a process in which a strand of nucleic acid joins or matches up with a complementary strand through the process of base pairing, wherein the process is basically used to locate or identify DNAs encoding specific proteins. It is well established in the art that 15-20 bases have been considered sufficient to achieve this process. The breadth of the claims includes nucleic acids of as little as 10 nucleotides. With these points in mind, it is the Examiners position that giving the claims their broadest reasonable interpretation, this language reads on an infinite number of possible DNA sequences for which there is not sufficient enablement.

The examples provided in the specification do not provide a representative number of different DNA sequences that would enable a representative number of the above discussed DNA sequences with assurances that can be used as probes or primers for the purpose of amplifying or detecting the PRO615 gene. The mere

recitation of this term, and the definitions provided do not serve as sufficient guidance to enable the breadth of the Claims for the various DNA sequences claimed. See Ex parte *Forman*, 230 USPQ 546. Since the first paragraph of the statute under 35 U.S.C. 112 requires that there must be an enabling disclosure to support the breadth of the Claims, a review of the specification confirms that the scope of the various DNA sequences that are discussed above have not been enabled. There is but a single nucleic acid disclosed with reference to PRO615, SEQ ID NO: 161. In the absence of sufficient guidance, it would require undue experimentation to enable a commensurate number of the sequences that are encompassed by the Claims.

With respect diagnostic applications or hybridization use, enablement is commensurate in scope only with claims to nucleic acids that are fragments of SEQ ID NO: 161, said fragments of sufficient length to be used as hybridization probes or primers. However, enablement is *not* commensurate in scope with fragments of nucleic acids that differ from SEQ ID NO: 161 due to codon degeneracy, as it is not recognized in the art to use such sequences that are degenerate for such detection or synthesis, and the specification provides no guidance as to how or why to make such degenerate primers. The specification also is not enabling of the breadth of claims to nucleic acid molecules that hybridize to the disclosed sequences.

7b. Claims 58-62 and 71-77 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as

to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to polynucleotides having at least 80%, 85%, 90%, 95% or 99% sequence identity with a particular disclosed sequence, or that merely hybridize to a disclosed sequence. The claims do not require that the claimed polynucleotide encode a particular protein, nor that any protein encoded thereby possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature The specification teaches that PRO615 has (unspecified) homology to Synaptogyrin. The structure of the putative PRO615 polypeptide is discussed at pages 2452 as having a type II transmembrane domain, corresponding to about amino acids 24-43, other transmembrane domains, corresponding to about amino acids 74-90, 108-126 and 145-161, respectively, and potential N-glycosylation site, corresponding to about amino acids 97-100. However, there is no functional characteristic associated with these motifs is provided, hence the mere observation that they exist is not probative of function or utility. Further, there is no disclosure that the protein is expected to be a transmembrane protein, nor of any extracellular domain.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity.

There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1616.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the human sequence.

Therefore, nucleic acids comprising the sequence set forth in SEQ ID NO: 161 or encoding the protein of SEQ ID NO: 162, or fragments thereof sufficiently long to be used as hybridization probes but not the full breadth of the claims meet the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Deposit requirement

8. Claims 58-63 and 70-77 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The deposit of biological organisms is considered by the Examiner to be necessary for enablement of the current invention (see 37 C.F.R.1.808(a)). Examiner acknowledges the deposit of organisms under accession number ATCC 209811 under terms of the Budapest Treaty on International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure in partial compliance with this requirement. However, in order to be fully compliant with the requirement, applicants must state that the deposit will be maintained for a term of at lest 30 years *and at least five (5) years after the most recent request for the furnishing of a sample of the deposit was received by the depository*. See 37 C.F.R.1.806.

Claim Rejections - 35 USC § 102

Priority is set at 4/28/99.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless :
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9a. Claims 58-67 and 71-73 are rejected under 35 U.S.C. 102(b) as being anticipated by Kedra et al., Accession NO: AJ002308, published 3-March-1998 (see PTO-1449 of 06/2003).

Kedra et al discloses a sequence that has 99.8% identity to nucleotides 24-1509 of SEQ ID NO: 161, a length of 1491 nucleotides (Appendix A). Kedra et al. describe the full-length cDNA. In addition, given this sequence identity the sequence of Kedra et al. would hybridize under stringent conditions to SEQ ID NO: 161. Kedra et al. also describe an amino acid sequence which is 224 amino acids long and identical to SEQ ID NO: 162 (see Appendix D). In addition, specification and Figure 61 describes the extracellular domain and the signal sequence. Thus, the nucleic acid sequence encoding the polypeptide of SEQ ID NO: 162, sequence lacking the signal peptide, extracellular domain of the polypeptide and sequence encoding the extracellular domain but lacking the signal peptide of SEQ ID NO: 162 are all anticipated by the reference. Therefore, claims 58-67 and 71-73 are anticipated by Kedra et al.

9b. Claims 58-62 and 71-77 are rejected under 35 U.S.C. 102(b) as being anticipated by Hawkins et al. (U.S. Patent No: 5, 854, 413).

Hawkins et al. discloses both nucleotide (SEQ ID NO: 1) and polypeptide (SEQ ID NO: 2) sequences that have substantial identity over SEQ ID NO: 161 and 162 of the instant invention. SEQ ID NO: 1 of Hawkins et al. has 99.7% similarity between nucleotides 26-910 (3 mismatches) of the instant invention SEQ ID NO: 161 (Appendix B). Similarly, SEQ ID NO: 2 of Hawkins et al. has 99.6% similarity between amino acids 1-224 (with a single mismatch) of the instant invention SEQ ID NO: 162 (Appendix C)). In addition, Hawkins et al. also describe vectors and host cells (see columns 13-15). Therefore, claims 58-62 and 71-77 are anticipated by Hawkins et al. (U.S. Patent No: 5, 854, 413).

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10a. Claims 74-77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kedra et al (1998, see PTO-1449 of 06/2003) in view of Hawkins et al. (U.S. Patent No: 5, 854, 413).

Kedra et al. describes the characterization of human synaptogyrin gene family. They have cloned the human SYNGR2 cDNA containing 1491 bp (ACC. NO: AJ002308). This sequence has 99.8% identity to nucleotides 24-1509 of SEQ ID NO: 161 of the instant invention (Appendix A, also see page 135 last paragraph). This covers the ORF of the gene, and is capable of encoding 224 amino acids, which is identical to SEQ ID NO: 162 of the instant invention (Appendix D, also see page 135 last paragraph). However, Kedra et al. does not teach the cloning into vectors for expression purposes.

Hawkins et al. describe vectors and host cells (see columns 13-15). Therefore, it would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to use the vectors and host cells as taught by Hawkins et al. to clone the nucleotides described in Kedra et al. The person of ordinary skill in the art would have been motivated to clone the nucleotides described by Kedra et al. into vectors and express in various host cells because this will allow the one of skilled in the art to conduct expression studies (see columns 30 and 31). There is a reasonable expectation of success because Hawkins et al. have expressed synaptogyrin homologs to study vesicular localization of these proteins (column 30, lines 57-60). Therefore, the

claims are obvious over Kedra et al (1998, see PTO-1449 of 06/2003) in view of Hawkins et al. (U.S. Patent No: 5, 854, 413).

11. No claim is allowed.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JS/04/04

LORRAINE SPECTOR
PRIMARY EXAMINER